II. Non-Technical Abstract

It is estimated that prostate cancer in the United States will be the leading male cancer diagnosis and the second most common cause of male cancer death in 1998. For patients diagnosed with prostate cancer, 10-15% of patients will have metastatic cancer at the time of diagnosis. Of patients undergoing radical prostatectomy, approximately 20-30% will have residual cancer cells remaining at the time the prostate is removed. Thus, a significant number of patients are at risk for a local re-growth of the prostate cancer. Additional patients may will develop metastatic prostate cancer some time after a definitive initial therapy (either surgery or radiation). The most common locations for prostate cancer spread are to the bones and lymph nodes. Removing or blocking the effects of the male hormone, testosterone, can slow the growth of prostate cancer. Currently there is no effective therapy available for these groups of patients and the need to develop new therapeutic approaches to treat advanced prostate cancer is clear.

This trial uses a gene therapy approach based on the "common cold" virus (adenovirus) to specifically target and kill prostate cancer. The virus has been altered to produce an enzyme (thymidine kinase) within prostate cancer cells that will be able to convert a safe antiviral medication (valacyclovir) to a intracellular poison. The poison then kills the prostate cancer cells. The ability to specifically target prostate cancer cells comes from the placement of a control element of DNA (osteocalin promoter) that functions in cells that have the ability to deposit calcium (bone, prostate cancer). The bone-like behavior of prostate cancer cells makes them particularly sensitive to this virus (Ad-OC-TK). This virus will be directly injected into a local recurrence or a distant metastasis using radiologic assistance. The injection will be repeated at one weeks time. A three week course of the valacyclovir will follow the initial injection. Therefore, by using a prostate cancer-specific control element of DNA (osteocalcin promoter) to produce thymidine kinase in prostate cancer cells, the trial hopes to demonstrate the ability this Ad-OC-TK to target and kill prostate cancer safely.

The trial describes a dose escalating Phase I trial to treat patients with recurrence of prostate cancer after surgical resection or metastatic prostate cancer. Patients enrolled will receive increasing ammounts of the virus. In the case of patients with post-surgical recurrence of prostate cancer, the site of recurrence will be injected under transrectal ultrasound or CT-guided imaging with the Ad-OC-TK. The group of patients with metastatic index lesion will be injected by interventional radiology with the guidance of either CT or plain radiographs dependent on location. One index lesion will receive two injections of the virus separated by one week and the patient will receive three weeks of valacyclovir from the time of the first injection. This treatment will be limited to one lesion per patient, so patients with multiple lesions will have one index lesion treated. The patients will be assessed for safety of this protocol, but serologic, tissue and radiologic evidence will be examined to confirm the biologic feasibility and the potential efficacy of this approach.